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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/402,820	10/12/1999	DANIEL G. CHAIN	20555/1203301-US1	6495

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EXAMINER	
DUFFY, PATRICIA ANN	

ART UNIT	PAPER NUMBER
1645	

DATE MAILED: 01/26/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/402,820	CHAIN, DANIEL G.	
	Examiner	Art Unit	
	Patricia A. Duffy	1645	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *4-22-04 amd 11-9-05*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *14,23-25 and 33-37* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14,23-25 and 33-37* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date *2003*.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Continued Examination Under 37 CFR 1.114

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on 4-22-04 has been entered.

Claims 1-13, 15-22 and 26-32 have been cancelled. Claims 14, 23-25 and 33-37 are pending and under examination.

Rejections Withdrawn

The rejection of claim rejected 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention is withdrawn in view of the cancellation of the claim.

Rejections Maintained

Claims 23 and 25 stand rejected under 35 U.S.C. 103(a) as being unpatentable over any one of Koing et al (Ann NY Acad. Sci., 777:345-355, 1996) or in view of Seubert et al (U.S. Patent 6,114,133, issued September 5, 2000 and filed November 14, 1994) and Duenas et al (BioTechniques, 16(3):476-483, 1994) is maintained for reasons made of record in Paper No. 10, mailed 5-23-01 the Office action mailed 4-22-04.

Applicant's arguments have been carefully considered but are not persuasive. Applicants again argue that there is no evidence that the antibody of Koing does not bind the precursor protein that is present in all cells and that the negative results indicate that the experimental conditions provided in the paper indicate improper conditions for binding. This again is not persuasive. The lack of staining is indicia that the antibody at issue does not bind the precursor. Applicants have provided no positive evidence that the antibody does in fact bind the precursor. Applicants argue the process of making the 286.8A

monoclonal antibody of Koing et al and that binding specificity to amino acids 3-8 indicates that is not free-end specific and would be expected to bind the precursor (at page 350 of Koing et al). This again is not persuasive, page 350 of Koing et al does not indicate that the antibody 286.8A was specific for amino acids 3-8. Further, it does not teach that the antibody bound the intact precursor from which it may be derived. Applicants argue other staining patterns with other antibodies. This is not persuasive, the issue is the antibodies of Koing et al as they relate to this rejection and evidence that the antibody used in the rejection does or does not bind the precursor from which it may be derived. Applicants argue hypothetical of experimental conditions of Koing et al as ineffective, however provides no extrinsic factual or side-by-side evidence that the antibody on which this rejection is based does in fact bind the precursor. The examiner maintains that the lack of binding indicates that the argued antibody does not bind the precursor and Applicants arguments are not persuasive. The issue is the instant antibody of the prior art. The teachings of Koing et al indicate that the antibody does not exhibit the binding pattern that is typical of monoclonal antibodies that bind the intact precursor (i.e. the significant amounts of intraneuronal immunoreactivity). Therefore, the examiner maintains the lack of such immunoreactivity As such, this rejection is maintained for reasons made of record.

Claims 14 stands rejected under 35 U.S.C. 103(a) as being unpatentable over Saido et al (The Journal of Biochemistry, 269(21):15253-15257, 1994, Fee-based IDS Nov 16, 2001) in view of Takeda Chemical Industries Ltd., (EP 0 683 234 A1, published November 22, 1995, reference AC on PTOL-1449 filed 12 October 1999) and Goding (Monoclonal Antibodies, Academic Press Inc., London 1983, pages 56-97) for reasons made of record in the Office Action mailed 4-22-04.

Claims 23, 24 and 35 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Saido et al (The Journal of Biochemistry, 269(21):15253-15257, 1994, Fee IDS Nov 16, 2001), Takeda Chemical Industries Ltd., (EP 0 683 234 A1, published November 22, 1995, reference AC on PTOL-1449 filed 12 October 1999) and Goding (Monoclonal Antibodies, Academic Press Inc., London 1983, pages 56-97) as applied to claims 14 and 32 above and further in view of Seubert et al (U.S. Patent 6,114,133, issued September 5, 2000 and filed November 14, 1994) and Duenas et al (BioTechniques, 16(3):476-483, 1994) for reasons made of record in the Office Action mailed 4-22-04.

Claims 33 and 34 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Saido et al (The Journal of Biochemistry, 269(21):15253-15257, 1994, Fee IDS of Nov 16, 2001) in view of Takeda Chemical Industries Ltd., (EP 0 683 234 A1, published November 22, 1995, reference AC on PTOL-1449 filed 12 October 1999), Seubert et al (U.S. Patent 6,114,133, issued September 5, 2000 and filed November 14, 1994) and Goding (Monoclonal Antibodies, Academic Press Inc., London 1983, pages 56-97) for reasons made of record in the Office Action mailed 4-22-04.

Claims 23, 25, 36 and 37 stand rejected under 35 U.S.C. 103(a) as being unpatentable over Saido et al (The Journal of Biochemistry, 269(21):15253-15257, 1994, Fee IDS of Nob 16, 2001) in view of Takeda Chemical Industries Ltd., (EP 0 683 234 A1, published November 22, 1995, reference AC on PTOL-1449 filed 12 October 1999), Seubert et al (U.S. Patent 6,114,133, issued September 5, 2000 and filed November 14, 1994) and Goding (Monoclonal Antibodies, Academic Press Inc., London 1983, pages 56-97) as applied to claims 33 and 34 above and further in view of Seubert et al (U.S. Patent 6,114,133, issued September 5, 2000 and filed November 14, 1994) and Duenas et al (BioTechniques, 16(3):476-483, 1994) for reasons made of record in the Office Action mailed 4-22-04.

Applicants traverse all of the rejections based on Saido et al together and as such, the rebuttal will be similarly presented. Applicant's arguments have been carefully considered but are not persuasive. Applicants argue that Saido et al teach polyclonal antibodies. This is not persuasive, one cannot show nonobviousness by attacking references individually where the rejections are based on combinations of references. See *In re Keller*, 642 F.2d 413, 208 USPQ 871 (CCPA 1981); *In re Merck & Co.*, 800 F.2d 1091, 231 USPQ 375 (Fed. Cir. 1986). Applicants argue for two pages the technicalities of monoclonal antibody production of the Specificaiton but not the references as combined. The immunogen of Saido et al was demonstrated to produce a polyclonal antibody with the requisite claimed binding specificity, which is the basis for the rejection. Applicant's arguments with respect to the methods of the specification have no bearing of the references as combined. The immunogen was known, the immunogen was demonstrated to produce polyclonal antibodies with the claimed specificity, and the secondary references provide motivation and conventional techniques to make the monoclonals and single chain antibodies with the desired specificity. Moreover, the claims are not limited to any specific species of monoclonal. Making monoclonal antibodies is highly routine in the art and the skilled artisan would be reasonably expected to achieve monoclonals and recombinant single chains as claimed in view of the success of the polyclonal of Saido et al and in view of the multiple other monoclonal antibodies made by the art to either the C-terminal end or N-terminal end of the beta amyloid peptide. Therefore, there is no unexpected amount of experimentation. Applicants followed routine procedures to achieve the expected result. Applicants argue that screening of 500 clones to get the desired clone is an unexpected amount of experimentation. This is not persuasive single hybridoma cell cloning is routinely done in multiple 96 well plates (see Celis et al, Production of Mouse Monoclonal Antibodies in "Cell Biology" Academic Press Inc., 1994; pages 273-276). Celis et al demonstrate cloning is done by plating multiple 96

well plates (see Figure 2). The screening of 5-96 well plates is not undue experimentation and highly conventional in the monoclonal antibody art. Applicants made monoclonal antibodies using mice, as are conventionally and routinely used in this art. Applicants argue that the C-terminal antibodies are not obvious because the N-terminus is physically and structurally distinct. This is not persuasive, the physiochemical differences of the C-terminal does not obviate the obviousness because other monoclonal antibodies that bind the C-terminal have been made. As such, since monoclonal antibodies have been made to the C-terminal, the differences in structure of the C-terminal and N-terminal do not preclude the obviousness of monoclonal antibodies with the claimed specificity therefore. Applicants argue that the differences in the structure preclude sequence accessibility and immunogenicity. This is not persuasive, there are numerous monoclonal antibodies of the art that bind the end of the C-terminal as is shown by the art of record. The rejections are maintained for reasons made of record.

Status of Claims

All claims stand rejected.

Conclusion

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within

TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Patricia A. Duffy whose telephone number is 571-272-0855. The examiner can normally be reached on M-Th 6:30 pm - 6:00 pm.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Smith Lynette can be reached on 571-272-0864. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Patricia A. Duffy

Primary Examiner

Art Unit 1645